Docket No.: 4619-009 PATENT

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

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| In re Application of | : | |
| Francis VANDERBIST | : | |
| U.S. Patent Application No. 09/424,247 | : | Group Art Unit: 1618 |
| | : | Allowed: |
| Filed: November 30, 1999 | : | Examiner: BERKO, RETFORD O |

For: DRY POWDER INHALER EXCIPIENT, PROCESS FOR ITS PREPARATION AND PHARMACEUTICAL COMPOSITION CONTAINING IT

**DECLARATION TRANSMITTAL LETTER**

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Enclosed is an executed *Rule 132 Declaration* in connection with the above-referenced application. We request that the record be clarified to acknowledge that the Declaration has been received and made of record.

Respectfully submitted,

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CERTIFICATION OF FACSIMILE TRANSMISSION
I HEREBY CERTIFY THAT THIS PAPER IS BEING FACSIMILE TRANSMITTED TO THE PATENT AND TRADEMARK OFFICE ON THE DATE SHOWN BELOW

KARYL WEST
TYPE OR PRINT NAME OF PERSON SIGNING CERTIFICATION

SIGNATURE 4-10-06 DATE

571-273-8300
FACSIMILE NUMBER

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of

Francis VANDERBIST et al.

U.S. Patent Application No. 09/424,247 : Group Art Unit: 1618

Filed: November 30, 1999 : Examiner: Retford O. Berko

For: DRY POWDER INHALER EXCIPIENT, PROCESS FOR ITS PREPARATION AND PHARMACEUTICAL COMPOSITION CONTAINING IT

Commissioner For Patents
P.O. Box 1450
Alexandria, VA 22313-1450

**DECLARATION UNDER 37 CFR 1.132**

Sir:

Now comes Francis Vanderbist, who states as follows:

1) I am one of the co-inventors of the present invention;

2) I have both training and many years of experience in the field of pharmaceutical chemistry;

3) I have conducted and/or supervised the following experiment and have demonstrated the unexpectedly superior pulmonary fraction of active ingredient made available from a dry powder inhaler (DPI) formulation when using anhydrous roller-dried β-lactose as an excipient as compared to spray-dried α-lactose monohydrate in a particle size range of from 150 to 250 µm.

Table 2 at page 12 of the present application describes the influence of the nature of lactose used as an excipient, i.e., anhydrous roller-dried β-lactose versus spray-dried α-lactose

monohydrate, and the particle size of these lactoses on the in-vitro deposition of L-lysine N-acetyl cysteinate (NAL).

The lactose particle size studied as described and evaluated in the present specification was between about 63µm and 150µm. A further experiment was conducted as described below using a lactose particle size between about 160µm and 250µm using NAL and another active substance.

EXPERIMENT

An experiment was performed using roller-dried anhydrous β-lactose and spray-dried α-lactose monohydrate with particle sizes comprised between 150µm and 250µm.

The two active drugs selected were NAL (ratio NAL/Lactose: 1/4) and Budesonide (ratio Budesonide/Lactose: 1/100).

Comparative in-vitro lung deposition of NAL and Budesonide using two different lactoses (roller-dried anhydrous β-lactose versus spray-dried α-lactose monohydrate) with the same particle size comprised between 150µm and 250µm.

The pulmonary fraction was measured using the multistage liquid Impinger at 100 l/min. during a period of 2.4 seconds, otherwise using the same procedure as described in the present specification. The results are shown below.

| Active Drug | Ratio Active/Lactose w/w | FPD in percent (%) Anhydrous roller dried β lactose 150-250 µm | Spray dried α - lactose monohydrate 150-250µm | Difference in Percent [%] |
|---|---|---|---|---|
| NAL | 1/4 | 28 | 25 | 12 |
| Budesonide | 1/100 | 31 | 24 | 29 |

The in-vitro fine particle dose (FPD) obtained with the formulation containing the roller-dried anhydrous β-lactose with a particle size comprised between 150 and 250µm is significantly greater (12% and 29% for NAL and Budesonide) than the one obtained with formulations containing the same active ingredient and spray-dried α-lactose monohydrate of the same particle size (150µ - 250µm).

This demonstrates the clear and unexpected superiority of the roller-dried β-lactose with a particle size comprised between 150 and 250µm to deliver active drugs from DPI formulations with an improved pulmonary fraction.

4) I am of the opinion that the above results would not have been expected by one skilled in the art at the time the present invention was made. This conclusion is further evidenced by the fact that such results would clearly not have been expected by one skilled in the art at the time the present invention was made in view of the prior art of record in this application.

5) Further, I am of the opinion that the above results are important and commercially significant.

6) I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these

statements were made with the knowledge that willful false statements and the like so made are punishable by fine, or imprisonment, or both, under *Section 1001 of Title 18 of the United States Code*, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Signature F. VANDERVIST

27 March, 2006

Date